

Promoting linear growth when treating child wasting

This article discusses the state of evidence surrounding the treatment of wasted and stunted children considering current challenges and possible solutions

Natasha Lelijveld is a Senior Nutritionist at ENN.

Kevin Stephenson is a Research Fellow at Washington University in St Louis USA.

Mark Manary is a Professor at Washington University in St Louis USA.



A mother feeds her malnourished twin boy with a fortified infant porridge at a health centre, Burkina Faso

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Key messages:

- Evidence suggests that children in wasting treatment are often stunted and they often become even more stunted during treatment and the post-discharge period.
- More research is needed to explore how wasting treatment programmes can better support linear growth and related functional outcomes.
- Current options for exploration include altering the composition and dose of ready-to-use food to contain more growth-promoting amino acids and the provision of better post-discharge support, since linear growth and development takes time to achieve.

Background

Wasted children are more likely to be stunted and vice versa. Wasting and stunting are both markers for, and drivers of, adverse outcomes throughout childhood, negatively impacting cognitive development and increasing the risk of morbidity and mortality due to infectious diseases, as well as of obesity and other metabolic complications in later life (Grey et al, 2021). Wasting treatment currently targets short-term outcomes including survival and weight gain. However, given the interrelated risks associated with wasting and stunting, treatment approaches may have the potential to simultaneously enhance linear growth in addition.

Over the past few decades, successful, multi-sector interventions to prevent stunting have been identified and the prevalence of stunting has reduced globally, albeit slowly (Hossain et al, 2017). Current evidence suggests that effective strategies for stunting reduction focus on preventing (rather than treating or reversing) linear growth retardation during the first 1,000 days of life (Leroy et al, 2020). Well-evidenced preventative interventions include micronutrient supplementation during pregnancy and early childhood, breastfeeding promotion, complementary feeding

education and complementary food supplementation such as regular small-quantity lipid nutrient supplements (Keats et al, 2021).

While stunting prevention should be prioritised, evidence also supports a biological plausibility for reversing stunting at the individual level. For example, adopted children who have experienced positive changes to their living environments have shown accelerated catch-up growth by aged 12 years (Johnson et al, 2018). Unfortunately, studies suggest that providing energy-dense and micronutrient-rich supplemental foods alone does not meaningfully support catch-up in height-for-age and more is needed to help children to achieve their growth potential (Dewey, 2016).

Linear growth during treatment for wasting

Survivors of severe wasting treatment are significantly more stunted than other stunted children in their community in the short- and long-term, regardless of how stunted they were at admission to treatment (Lelijveld et al, 2016). This suggests that children's height-for-age declines while receiving treatment for wasting. The lack of adequate, subsequent catch-up growth

also implies that the effects of wasting linger even after anthropometric 'recovery' is achieved. Alternative approaches to wasting treatment are needed that reduce the risk of stunting during recovery from wasting and, ideally, support catch-up in linear growth and development.

Route forward: Better supplementation?

One possible route forward is more targeted and comprehensive supplementation which specifically influences the biological drivers of growth. Evidence shows that essential amino acids regulate a complex set of molecular pathways involving a central signalling node (mTORC1) and the growth hormone IGF-1. These work together to control growth by promoting tissue building and preventing tissue breakdown (Semba et al, 2016; Valvezan & Manning, 2019). Without key amino acids, mTORC1 cannot be activated (Peterson et al, 2011). Stunted children have lower levels of all essential amino acids and likely require higher levels than many non-stunted children due to the need for catch-up growth. Animal-source foods are the richest sources of essential amino acids but are often lacking in the diets of children from countries with high burdens of stunting (Dror & Allen, 2011).

Greater availability of amino acids is also needed to fight systemic inflammation which often affects wasted and stunted children (Maleta et al, 2021). Targeting the various causes of inflammation in stunted children may also be essential for its reversal. While such avenues provide opportunities for reversing linear growth faltering, it is important to note that catch-up in linear growth does not necessarily reflect recovery in other domains, such as brain development, structure and function (Mackes et al,

2020). However, improved amino acid supplementation and the control of inflammation provide potential hypotheses for how wasting treatment can contribute to the prevention and reversal of stunting, ideally with subsequent functional implications.

Altering the composition and dose of ready-to-use food (RUF) might be important for promoting linear growth during and after wasting treatment. Providing milk-containing RUFs has been consistently associated with improved weight gain but less consistently with gain in length (Potani et al, 2021). The IGF-1 promoting effect of dairy has been proposed as a possible mechanism underlying this finding, while it is also possible the improved amino acid content might play a role through mTORC1. Dosage of RUF may also be important for linear growth, since wasting studies that have explored a reduced dosage regime have seen similar weight gain to the current dosage regime but reduced linear growth velocity (Kangas et al, 2019). In two studies, the rates of weight gain and recovery were similar in the standard dose and reduced dose groups, suggesting that the reduction in linear growth velocity may result from inadequacies in specific nutrients rather than insufficient wasting treatment (Stephenson et al, 2021). Identifying which nutrients are implicated could contribute to a better under-

standing of what causes declines in height-for-age z-scores after wasting recovery.

Route forward: Better post-discharge care?

In addition to maximising the formulation and dosage of RUF, post-discharge care following wasting treatment may mitigate the extent of further stunting. Wasting treatment is usually provided for a relatively short period (maximum 16 weeks) until adequate weight gain is achieved. Adequate weight is a prerequisite for linear growth attainment (Isanaka et al, 2019). Therefore, continuing wasting support beyond adequate weight gain may support linear growth and other longer-term outcomes. We know that current post-discharge care is inadequate with high rates of post-discharge mortality and relapse observed in many settings (Stobaugh et al, 2019; O'Sullivan et al, 2018). We also know that children are not immunologically recovered at discharge from wasting care, even if they have achieved adequate weight gain (Njunge et al, 2020). While the evidence for post-discharge vulnerability in severe wasting survivors is strong, very few studies have explored the impact of post-discharge interventions (Noble et al, 2021). The limited data available suggest that providing antibiotics, prebiotics/synbiotics, and/or psychosocial stimulation post-discharge

may be beneficial for growth, survival and development. Post-discharge food supplementation and cash transfers may also reduce relapse (Mengesha et al, 2016; Grellety et al, 2017). These interventions have the potential to support long-term growth and development in wasting survivors. However, more robust and large-scale trials are needed.

Conclusion

Wasting and stunting have interrelated risk factors and an episode of wasting, even with treatment, can exacerbate stunting in the short-term and fail to support adequate catch-up growth in the longer-term. Current evidence suggests that optimising RUF formulations, especially those with adequate essential amino acids to activate biological growth pathways, optimising RUF dosage, increasing the intake of animal-source foods and better post-discharge support may contribute to optimal linear growth in children who survive wasting. However, this research is in its infancy and further exploration into optimal strategies that simultaneously target wasting and stunting is needed. Better still, more effective prevention strategies for wasting and stunting are needed.

For more information, please contact Natasha Lelijveld at natasha@enonline.net

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